A Ferrocene Derivative Redox Sensor for Mercuric Ion: Synthesis and Electrochemical Study

Nhat-Nguyen Bui, Jong-Tai Hong, Sun-il Mho, and Hye-Young Jang*

Division of Energy Systems Research, Ajou University, Suwon 443-749, Korea. *E-mail: hyjang2@ajou.ac.kr

Received May 21, 2008

Key Words : Ferrocene, Mercuric ion, Electrochemistry, Redox sensor

The sensitive detection of mercuric ion is currently a task of prime importance for environmental or biological concerns. To develop sensitive mercuric ion sensors, various receptors consisting of a mercuric ion recognition unit and a probe exhibiting physical responses upon the coordination of mercuric ion have been reported. Among them, ferrocene derivatives are often applied to redox sensors due to the unique electrochemical property. In the presence of mercuric ions, the ion-recognition event induces the significant electrochemical changes at the redox active ferrocenyl moiety. In addition, the ease of functionalization of ferrocene leads to the synthesis of assorted ferrocene derivatives possessing the metal ion binding unit. Recently, our research has focused on the development of new ferrocene complexes as redox sensors for the mercuric ion detection. In this account, we report the synthesis and electrochemical analysis of 2-(ethylthiomethyl)-N-ferrocenylmethyl aniline in the presence of various metal ions, illustrating this ferrocene complex as a sensitive and selective redox sensor for the detection of mercuric ion.

As shown in Scheme 1, 1-(bromomethyl)-2-nitrobenzene 1 was treated with ethanthiol with sodium metal to afford ethyl(2-nitrobenzyl)sulfide 2 in 72% yield. Subsequent reduction of compound 2 provided 2-(ethylthiomethyl)aniline 3 which reacted with ferrocene carboxaldehyde 4, forming imine 5. Due to the instability of compound 5 on the silica gel, compound 5 was not isolated and subject to the reduction conditions using NaB(OAc)₃H to give 2-(ethylthiomethyl)-N-ferrocenylmethyl aniline 6 in 80% yield.

With compound 6 in hand, electrochemical properties of compound 6 were evaluated in the absence of any metal ion via cyclic voltammetry (CV). In the range of 0.0 to 2.0 V, two oxidation peaks appear at 0.41 V and 1.04 V during the anodic scan, and no reduction peak was observed in the reverse scan, shown in Figure 1. When the anodic scan was reversed at 0.80 V subsequent to the 1st oxidation at 0.41 V, the reversible reduction peak at 0.30 V was detected, with the peak separation of ca. 0.11 V. Accordingly, the first oxidation peak at 0.41 V was speculated to be the oxidation of the ferrocene entity of compound 6. The second oxidation peak at 1.04 V is likely due to the oxidation of the thioether unit.
peak at 1.04 V was attributed to the oxidation of amine functional group. In light of previous reports regarding the electrochemical oxidation followed by irreversible chemical reaction of the amine group affording aldehydes or nitrile,3,4 the irreversible second anodic wave was attributed to the electrochemical reaction and subsequent irreversible chemical reaction of amine of compound 6.

Subsequent to the electrochemical study of metal free compound 6, the CVs of compound 6 in the solution containing different concentrations of mercuric ion were obtained (Figure 2). Upon increasing the concentrations of mercuric ion, the anodic peak of Fc/Fc+ redox couple of compound 6 at 0.41 V was severely shifted toward cathodic direction to 0.19 V (cathodic shift $\Delta E = -0.22$ V), which was ascribed to the weak interaction of sulfur in compound 6 with mercuric ion. The cathodic shift of the redox couple of ferrocene derivatives induced by the weak interaction of metal ions was previously reported by Guo and co-workers.5

In addition to the cathodically shifted peak of the Fc/Fc+ redox couple of compound 6, a new Fc/Fc+ redox couple peak at 0.33 V stemming from the binding of compound 6 and mercuric ion appeared as shown in Figure 2. Due to the cationic nature of compound 6 through the binding with mercuric ion, the oxidation potential wave of mercuric ion bound compound 6 was anodically shifted to 0.33 V from the oxidation potential of 0.19 V of the metal free compound 6. The newly formed redox waves exhibited ca. 0.096 V separation between the anodic and cathodic peaks, showing quasi-reversibility. Noticeably, as the concentration of mercuric ions was increased, the current of the new potential wave was continuously growing. On the other hand, the current of the potential wave of metal free compound 6 was gradually reduced. The equilibrium constant ratio indicating the binding affinity difference of compound 6 and 1 electron oxidized compound 6 toward mercuric ion was evaluated, using the well-known equation correlating the electrochemical potential with the thermodynamic value (eq. 1).6

Inserting the half wave potential difference value, $\Delta E (0.14$ V, $E_{1/2}^\text{complex} - E_{1/2}^\text{free ionophore}$) calculated from the CVs of compound 6 with/without mercuric ion, the ratio of the complex formation constants $K_{\text{neutral}}/K_{\text{ox}}$ was calculated to be 233. Resulting equilibrium constant ratio means that the unoxidized compound 6 is 233 times stronger binding to mercuric ion than 1 electron oxidized compound 6.

$E_{1/2}^\text{complex} - E_{1/2}^\text{free ionophore} = (RT/nF)\ln(K_{\text{neutral}}/K_{\text{ox}}) \quad (1)$

Subsequent to the electrochemical study in the range of 0.0 V to 0.8 V, the anodic scan was expanded to 2.0 V to investigate the changes of the second anodic peak at 1.04 V corresponding to the amine in compound 6 in the presence of high concentration of mercuric ion. As illustrated in Figure 3, the second oxidation peak of compound 6 disappeared upon the addition of mercuric ions. Accordingly, the tight binding of mercuric ion to compound 6 is speculated to occur at the amine unit. Sulfur together with nitrogen in compound 6 is also assumed to cooperatively bind mercuric ion. In addition to the significant decrease in the oxidation current of the second anodic wave of compound 6, a sharp anodic peak was observed at 0.38 V upon the addition of 0.75 equivalents of mercuric ion as shown in Figure 3. With high concentrations of mercuric ion added, unbound mercuric ion is assumed to be reduced at the surface of electrode in the negative potential region, where the reduced mercury
The combination of electrochemically active ferrocene carboxaldehyde and 2-(ethylthiomethyl)aniline as a metal ion recognition site has formed 2-(ethylthiomethyl)-N-ferrocenylmethyl aniline, a sensitive and selective electrochemical sensor for Hg\(^{2+}\). Both nitrogen and sulfur of compound 6 participate in the mercuric ion binding cooperatively. The coordination of mercuric ion affects the electronic environment of the ferrocene entity proximal to nitrogen and sulfur, forming a new anodically shifted Fe/Fe\(^{n+}\) redox couple. The potential difference between metal free compound 6 and Hg\(^{2+}\) bound compound 6 was used to understand the quantitative binding ability of compound 6 toward Hg\(^{2+}\). In contrast to Hg\(^{2+}\), the Fe/Fe\(^{n+}\) redox couple of compound 6 with Zn\(^{2+}\), Co\(^{2+}\), Cd\(^{2+}\), or Mg\(^{2+}\) did not show noticeable changes of potential waves, illustrating the selectivity of compound 6 to Hg\(^{2+}\).

**Experimental**

Anhydrous solvents were transferred by an oven dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Dichloromethane and 1,2-dichloroethane were distilled from calcium hydride. THF was distilled from benzophenone ketyl, Acetonitrile was purchased from Fluka and distilled from calcium hydride. Ethanol and methanol were distilled from sodium metal. Proton nuclear magnetic resonance (\(^1\)H NMR) spectra were recorded with a Varian Mercury plus (400 MHz) spectrometer. Chemical shifts are reported in delta (\(\delta\)) units, part per million (ppm) downfield from trimethylsilane. Coupling constants are reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (\(^{13}\)C NMR) spectra were recorded with a Varian Mercury plus (400 MHz) spectrometer. Chemical shifts are reported in delta (\(\delta\)) units, part per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. Elemental analysis was carried out at the Inter-University Center Natural Science Facilities, Seoul National University. Electrochemical data were recorded on a potentiostat/galvanostat (PARC (Princeton Applied Research), model 263) with Electrochemistry Power Suite Module and Cyclic voltammetry software. The three-electrode cell consisting of Pt disc (the working electrode), Ag wire (the pseudo reference electrode), and Pt wire (the auxiliary electrode) was employed. Compound 6 (0.01 M) were dissolved in CH\(_3\)CN solution containing 0.1 M LiClO\(_4\). The resulting solutions were subject to cyclic voltammetry experiments at a scan rate of 100 mV/s. Compound 2\(^5\) and 3\(^6\) exhibited spectral properties consistent with previous literature reports.

2-(Ethylthiomethyl)-N-ferrocenylmethyl aniline 6: 2-(ethylthiomethyl)aniline 3 (67 mg, 0.4 mmol) was dissolved in the dichloromethane solution (2 mL) of ferrocene carboxaldehyde 1 (95 mg, 0.48 mmol) and molecular sieve. The mixture was refluxed for 12 hrs under the nitrogen atmosphere. After being cooled to room temperature, the solution was filtered through Celite and the filtered solution was evaporated. This mixture was dissolved in 1,2-dichloroethane (5 mL), and subsequently NaB(OAc)\(_3\)H (101 mg, 0.48 mmol) was added. The reaction mixture was allowed to stir overnight at room temperature. The solution was diluted with CH\(_2\)Cl\(_2\) (2 × 10 mL), extracted with saturated NaHCO\(_3\) (15 mL), and washed with water (2 × 10 mL). The organic layer dried over MgSO\(_4\) and the solvent was evaporated. The purification was conducted via flash column chromatography.
graphy (SiO₂, 20:1, hexanes:ethyl acetate) to provide 6 (116 mg, 0.32 mmol) as a yellow oil in 80% yield. TLC Rf = 0.74 (3:1, hexanes:ethyl acetate). ¹H NMR (CDCl₃, 400 MHz) δ = 7.19 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 6.0 Hz, 1H), 6.70 (m, 2H), 4.74 (br, 1H), 4.28 (s, 2H), 4.22 (s, 5H), 4.15 (s, 2H), 4.01 (s, 2H), 3.77 (s, 2H), 2.45 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 3.2 Hz, 3H) ppm. ¹³C NMR (CDCl₃, 100 Hz) δ = 146.5, 130.6, 128.7, 121.3, 116.9, 111.2, 86.5, 68.8, 67.9, 67.6, 43.2, 33.8, 25.4, 14.8. FABMS 365.0900 calcld for C₂₀H₂₃FeNS; Found, 365.0900. FTIR (KCl) 3350, 3091, 2964, 2853, 1604, 1509, 1461, 1261, 1311, 1105, 820, 745 cm⁻¹.

Acknowledgments. This work was in part supported by the Korea Science and Engineering Foundation (grant No. R01-2007-000-20223-0).

References